Activation of the Caudal Anterior Cingulate Cortex Due to Task-Related Interference in an Auditory Stroop Paradigm

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Abstract: Successful information processing requires the focusing of attention on a certain stimulus property and the simultaneous suppression of irrelevant information. The Stroop task is a useful paradigm to study such attentional top-down control in the presence of interference. Here, we investigated the neural correlates of an auditory Stroop task using fMRI. Subjects focused either on tone pitch (relatively high or low; phonetic task) or on the meaning of a spoken word (high/low/good; semantic task), while ignoring the other stimulus feature. We differentiated between task-related (phonetic incongruent vs. semantic incongruent) and sensory-level interference (phonetic incongruent vs. phonetic congruent). Task-related interference activated similar regions as in visual Stroop tasks, including the anterior cingulate cortex (ACC) and the presupplementary motor-area (pre-SMA). More specifically, we observed that the very caudal/posterior part of the ACC was activated and not the dorsal/anterior region. Because identical stimuli but different task demands are compared in this contrast, it reflects conflict at a relatively high processing level. A more conventional contrast between incongruent and congruent phonetic trials was associated with a different cluster in the pre-SMA/ACC which was observed in a large number of previous studies. Finally, functional connectivity analysis revealed that activity within the regions activated in the phonetic incongruent vs. semantic incongruent contrast was more strongly interrelated during semantically vs. phonetically incongruent trials. Taken together, we found (besides activation of regions well-known from visual Stroop tasks) activation of the very caudal and posterior part of the ACC due to task-related interference in an auditory Stroop task. *Hum Brain Mapp 00:000–000, 2009.* © 2009 Wiley-Liss, Inc.

Key words: Stroop task; attention; interference; cognitive control; inhibition; anterior cingulate; prefrontal cortex; functional connectivity

INTRODUCTION

Since the Stroop effect was first described more than 70 years ago [Stroop, 1935], it became one of the most intensively studied phenomena in cognitive neuroscience and still has a key role in the study of attentional top-down mechanisms [for reviews see Dyer and Severance, 1973; MacLeod, 1991]. In spite of many variations of the Stroop task, the basic principle of word reading and color detection has not changed over the decades and is still widely

used. In the standard Stroop task, subjects are asked to name the colors of compatible and incompatible color-words and of control patches, e.g., solid color squares. Stroop interference corresponds to the difference between the reaction times in the incongruent and the control condition. The interference effect and significant reaction time increase during the incongruent trials is accompanied by a facilitation effect for the congruent trials, reflected by a decrease in reaction times, although facilitation is considered to be a somewhat weaker phenomenon than interference [MacLeod, 1991].

During the last two decades, the Stroop task was implemented using neuroimaging techniques, such as PET and fMRI, and revealed functional neural networks involved in the control of Stroop interference [e.g., Carter et al., 1995; Leung et al., 2000; Pardo et al., 1990; Peterson et al., 1999]. The Stroop interference task seems to principally rely on the activity of a limited number of key regions, in spite of the fact that the experimental designs evolved to numerous specializations. According to the standard theory, the anterior cingulate cortex (ACC) signals frontal regions, such as the dorsolateral prefrontal cortex (DLPFC), to further increase the attentional bias toward task-relevant processing when distracting stimulus properties cause a task-related conflict. Consequently, recent studies showed a major interest in the ACC and DLPFC, which emerged as the two anatomical regions playing the most important role in the control of conflict management [e.g., Banich et al., 2001; MacDonald et al., 2000; Milham et al., 2001].

Several studies have addressed theories of ACC functions related to different cognitive abilities, such as, for example, conflict monitoring [Botvinick et al., 1999, 2001; Carter et al., 2000; Kerns et al., 2004; MacDonald et al., 2000], error detection [see reviews Bush et al., 2002; Gehring and Knight, 2000], and response selection [Erickson et al., 2004; Milham et al., 2003; Paus, 2001]. In addition, the DLPFC has been shown to contribute to cognitive control function [MacDonald et al., 2000; Miller and Cohen, 2001].

In this study, we implemented an auditory Stroop interference task using fMRI. Several studies demonstrated the applicability of the Stroop interference task in the auditory domain behaviorally [Leboe and Mondor, 2007; McClain, 1983; Shor, 1975]. In one version, not only were stimuli presented in auditory modality, but subjects were also either required to respond by naming a word or producing a hum with different pitch [McClain, 1983]. This paradigm indicated that interference was at least partially attributable to response inconsistency, as suggested by the response incompatibility theory [Treisman and Fearnley, 1969]. In our paradigm, however, responses were neither given by spoken words nor by hummed tones, but by button presses. In this context, another source of interference is more relevant: Stroop conflict arises if responses have to be given according to that one of two contrasting item features, which is processed slower and less automatic, such as color or pitch naming, in the presence of inconsistent semantic information. Conflict is smaller or absent if responses are given according to the faster and more automatically processed item feature, such as word meaning in the presence of inconsistent color or pitch information. This asymmetry predicts that in our task, interference should be larger if subjects are required to respond to a pitch in the presence of incongruent semantic information when compared with when they are required to respond to the meaning of a word in the presence of incongruent pitch information.

Our motivation for implementing the auditory Stroop approach with functional imaging was fourfold as follows:

Selective attention might be different in the auditory when compared with the visual domain. Most applications of the Stroop interference task were designed using visual stimuli and revealed variations of activity in the anterior ACC and DLPFC. We addressed the question of whether the functional network activated by conflict processing represents a common system or whether there are specific alterations regarding the sensory modality. We expected the behavioral results and the conflict network activations to generally follow the common Stroop findings, but hypothesized prominent differences due to the new sensory modality for two reasons. Firstly, because the visual and the auditory pathways include fundamentally different processing steps for sensory input [Hendee and Wells, 1997; Handel, 1989]. Secondly, because alterations of activations in ACC due to different cognitive processes are well described in the fMRI literature, e.g., in the context of conflict processing and movement execution [Picard and Strick, 2001], attention and stimulus detection [Posner and Petersen, 1990], and emotional processing [Bush et al., 2000; Devinsky et al., 1995]. To further investigate the integration of activity within the conflict network and to reveal its adjustments due to the auditory modality, we additionally performed a functional connectivity analysis using the "psychophysiological interaction" approach [Friston et al., 1997].

In most investigations of the Stroop effect, interference effects are being analyzed by the contrast between incongruent and congruent (or neutral) stimuli in a color-naming task (where the processing of semantic information has to be suppressed). This contrast involves interference already at the sensory level of processing as well as at higher levels. The contrast between incongruent items in the color naming and incongruent items in the color reading task has rarely been investigated. However, this latter contrast does not involve interference at a sensory level, because stimuli are exactly identical in the two conditions and only task demands differ (in other words, conflict at the level of sensory processing is "substracted out"). Because this contrast reveals more directly interference at higher processing levels, we aimed at comparing it with the more conventional "incongruent > congruent" contrast.

There is an ongoing discussion regarding the role of priming in the Stroop task. A center of debate in recent stud-

ies involving conflict-adaptation is the controversy of the conflict theory versus priming-effects. It is still unclear if reaction time decreases related to repetitions of equal stimuli during a conflict task are actually caused by the greater recruitment of top-down conflict monitoring or should rather be attributed to episodic memory or stimulus-specific repetition priming as shown for Flanker-tasks [Mayr et al., 2003; Nieuwenhuis et al., 2006].

An auditory Stroop approach could be useful for clinical purposes. Abnormal conflict management was evidenced for several brain disorders, e.g., attention-deficit/hyperactivity disorder [for review see Lansbergen et al., 2007] or in paranoid schizophrenia [Nordahl et al., 2001]. An auditory approach to the common Stroop interference task seems of particular interest since the auditory sense is especially affected in psychiatric disorders such as schizophrenia [Veuillet et al., 2001]. Recently, it has been reported that an increased Stroop effect can serve as a marker for a genetic vulnerability to schizophrenia [e.g., Becker et al., 2008; Filbey et al., 2008]. Because schizophrenic patients have deficits in both auditory processing and conflict monitoring, an auditory version of the Stroop task might provide an even more sensitive trait marker for schizophrenia.

METHODS

Participants

A total of 29 healthy subjects (14 women; age 18–34, mean age ± s.d.: 27.0 ± 7.4 years; and handedness: 22 right, 7 left) participated in the study. They were recruited from the University of Bonn as well as via newspaper. The study was approved by the local medical ethics committee, and all subjects provided written informed consent.

Experimental Procedures

We used an auditory version of the Stroop task [Stroop, 1935], where subjects were presented the German equivalents of the words "high" and "low" (German: "Hoch," "Tief") in either a high or low tone pitch. In each of the two identical blocks of the paradigm, subjects performed first the semantic condition, where they indicated via button press whether the word "high" or "low" was presented, regardless of the tone pitch. In the consecutive "phonetic" condition, the subjects were asked to decide if the word was presented in a high or low tone pitch, regardless of the word meaning. As an additional control, we presented the word "good" (German: "Gut") either in a high or in a low tone pitch in both conditions. In the semantic condition, subjects were instructed not to press a button in these trials. These trials did not enter further analysis. Only the control trials in the phonetic condition were subsequently analyzed. Only trials with correct responses entered into the contrasts of the second level
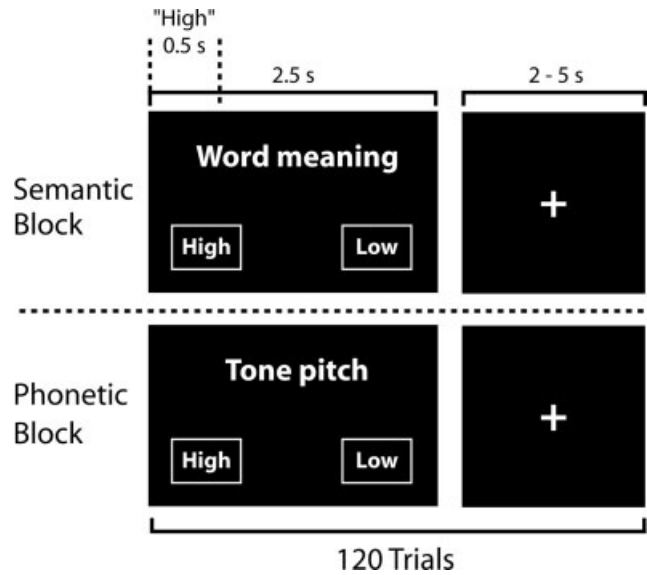

Figure 1.
Overview of the paradigm.

general linear model. An overview of the paradigm is depicted in Figure 1.

The sound files were spoken and digitalized by one of the experimenters, and transposed to a high or low tone pitch (tone difference of a quint), respectively, aligned in frequency using the Entropic Timescale Modification ($ETSM^{TM}$) as included in the "Goldwave" audio editing software (http://www.goldwave.com/). This transformation guaranteed equal length of all sound files (500 ms).

Test Session

Subjects completed a total of 480 trials while they were being scanned in fMRI. Prior to the start of the experiment, subjects went through at least 10 practice trials or more, if necessary. The experiment was divided into two parts of 240 trials each to ascertain a stable level of attention during the entire length of the paradigm. Subjects were allowed to leave the scanner between the two parts. Every part was subdivided into two blocks, each with 120 trials for the semantic block and 120 trials for the phonetic block. Every block contained all three sound files ("high," "low," and "good") in either a high or low tone pitch. Each of these six conditions was presented in 20 trials. The words "word meaning" and "tone pitch" were presented on the screen in all trials for the sake of clarity. Words were presented for 500 ms, and the subjects were asked to answer as fast as possible during the consecutive 2,000 ms interval. All trials with response delays longer than 2,500 ms were discarded. Trials were administered in a randomized, counterbalanced order across subjects. The 2,500 ms trial was followed by a pause of 2,000–5,000 ms length, during which a fixation cross was shown. Stimuli were

presented using Presentation® software (Version 0.71; Neurobehavioral Systems; Albany, CA) via MRI-compatible liquid-crystal display (LCD) goggles and MRI-compatible electrostatic headphones (both NordicNeuroLab, Bergen, Norway), and responses were obtained through a fiber optic magnetic resonance-compatible control pad.

MRI Data Acquisition

Thirty-eight axial slices were collected in a 1.5T scanner (Avanto, Siemens, Erlangen, Germany). We collected 1160 T2*-weighted, gradient echo (EPI) scans (slice thickness: 3 mm; interslice gap: 0.48 mm; matrix size: 64 × 64; field of view: 222 mm; echo time: 35 ms; and repetition time: 2,500 ms). Thereafter, we acquired a sagittal T1-weighted MPRAGE sequence for each subject for anatomical localization (number of slices: 160; slice thickness: 1 mm; inter-slice gap: 0.5 mm; matrix size: 256 × 256; field of view: 256 mm; echo time: 3.09 ms; and repetition time: 1,660 ms).

fMRI Analysis

Analysis was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.63, part of FSL software (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) using standard procedures. The following prestatistics processing was applied: motion correction using MCFLIRT [Jenkinson et al., 2002]; slice-timing correction using Fourier-space time-series phase-shifting; nonbrain removal using BET [Smith, 2002]; spatial smoothing using a Gaussian kernel of FWHM 6 mm; mean-based intensity normalization of all volumes by the same factor; and highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0 s). Time-series statistical analysis was carried out using FILM [Woolrich et al., 2001]. Registration to high resolution and/or standard images was carried out using FLIRT [Jenkinson et al., 2002]. Preprocessed data were fitted by the convolution of multiple regressors with a canonical hemodynamic response function to obtain parameter estimates for each condition covariate. The fMRI-analysis used a set of seven regressors, each of 1,000 ms duration. Four regressors were used for the congruent (pitch: "high"/meaning: "high" or "low/low"), and incongruent ("high/low" or "low/high") trials in the semantic and phonetic blocks of the paradigm (i.e., (1) congruent semantic; (2) incongruent semantic; (3) congruent phonetic; and (4) incongruent phonetic). Two regressors were used for the control-condition ("good") in the semantic and phonetic block, and one regressor for the trials with incorrect responses. Incorrect responses were modeled because otherwise variance of the associated BOLD responses would contribute to the implicit baseline activity and deteriorate the estimation of the other regressors' beta values. To control for repetition effects, the fMRI analysis was carried out a second time with the same set of regressors, with the only exception that each repetition of a trial in the same category (congruent–congruent or incongruent–incongru-

ent) was modeled with the same regressor as the incorrect trials, therefore, excluding them from the relevant contrasts. A third analysis was carried out, where instead of excluding repeating trials for every subject, the same amount of randomly chosen trials was excluded from the relevant contrasts of the second level general linear model, by moving them to the regressor for incorrect trials.

The comparison of activations was carried out by extracting activation values from, e.g., the "incongruent phonetic > incongruent semantic" contrast for all three analyses. We used an inclusion mask defined by the activated regions of the first analysis on significance level (Z = 3.1; P = 0.001) to specify activations entering the other two analyses.

P values in the ANOVAs were Huynh-Feldt corrected for inhomogenities of covariance when necessary [Huynh and Feldt, 1976]. Images are displayed by neurological convention, with left side corresponding to the left hemisphere. Effects are significant at P < 0.001 and at a cluster size of 10 or more contiguous voxels. Mean parameter estimates for the different conditions are shown for all contrasts (ordinate in arbitrary units). Error bars represent s.e.m.

We added the locations of 112 ACC activations to our contrast in Figure 4A-2 using coordinates from a review by Barch et al. [2001]. The activations were collected from tasks falling under the categories of response inhibition, underdetermined responding, and commission of errors (e.g., Stroop, Go/No-Go, and Flanker-tasks). The stereotactic coordinates referring to the Talairach coordinate system were transformed to MNI coordinates using the tal2mni.m script available from M. Brett. (http://eeg.sourceforge.net/doc_m2html/bioelectromagnetism/tal2mni.html). The result is shown in Figure 4B. For greater clarity, we used the perpendicular line on the intersection of the bicommissural line (AC-PC) through the anterior commissure as an additional orientation border.

Functional connectivity with the ACC was calculated by using activity within the functional ROI in the posterior ACC region (Fig. 4A-2) resulting from the "Phonetic > Semantic"-contrast, thereby identifying brain regions showing significant covariation or functional connectivity with this seed location. We used a sphere with 6 mm diameter centered on the peak voxel as a seed region. The functional connectivity analysis was conducted using the "psychophysiological interaction" method [Friston et al., 1997]. The method we used relies on correlations in the BOLD time series data and makes no assumptions about the nature of the neural activity that may have contributed to the BOLD signal. We extracted the entire time-course of activity of each individual subject and multiplied that time course with a condition vector that was ones for five TRs following each trial type, and zeros otherwise. These resulting vectors were then used as covariates in a separate regression. Analyses were performed for each subject individually and were subsequently entered into a group-level analysis.

TABLE I. Descriptive statistics of behavioral data

Condition	Reaction time (ms)	s.e.m (ms)	Errors (%)	s.e.m (%)
Semantic-congruent	793	38	2	1
Semantic-incongruent	794	46	2	1
Phonetic-congruent	789	40	4	1
Phonetic-incongruent	906	52	11	3
Control	854	48	9	3

RESULTS

Behavioral Results

The auditory Stroop design created a robust Stroop interference effect. A two-way ANOVA with "congruency" and "semantic-phonetic" as repeated measures revealed main effects of each factor ("congruency": $F_{1,28} = 10.15$, $P = 0.004$; "semantic-phonetic": $F_{1,28} = 43.31$, $P < 0.001$) and a significant "congruency" × "semantic-phonetic" interaction ($F_{1,28} = 107.38$; $P < 0.001$). As expected, the incongruent phonetic trials turned out to be the critical condition of top-down conflict processing in this Stroop task, producing significantly longer reaction times compared with the other conditions (incongruent phonetic trials: 906 ms (s.e.m. 52 ms), other conditions: < 800 ms (s.e.m. < 45 ms), each $P < 0.001$, each $t_{28} < 6.14$; two-tailed t tests; for detailed behavioral data, see Table I, Fig. 2A). In the phonetic control condition using the word "good," subjects had a reaction time of 854 ms (s.e.m. 48 ms), which differed significantly from the other conditions (each $P < 0.001$, each $t_{28} < 6.2$; two-tailed t tests) and was almost at the exact half between the reaction times of the condition of highest conflict (incongruent phonetic) and the others.

The error rates confirmed the results of the reaction times. Again, Stroop interference was maximal in the incongruent-phonetic condition, as the error rate was significantly higher (11%, s.e.m. 3%) when compared with the other conditions (<5%; Fig. 2B). A two-way ANOVA with "congruency" and "semantic-phonetic" as repeated measures revealed main effects of each factor ("congruency": $F_{1,28} = 10.72$, $P = 0.003$; "semantic-phonetic": $F_{1,28} = 12.23$, $P = 0.002$) and a significant "congruency" × "semantic-phonetic" interaction ($F_{1,28} = 10.01$; $P = 0.004$). Pair-wise t tests showed that error rates in the "incongruent-phonetic" condition were larger than in any other condition ($P < 0.05$, $t_{28} > 4.82$; two-tailed t tests).

A common observation during the Stroop task is that processing of incongruent stimuli is facilitated by previous processing of incongruent stimuli, which has been explained by behavioral adjustments [Botvinick et al., 2001]. Thus, an incongruent trial following an incongruent trial (iI) should result in faster reaction times than on incongruent trials following congruent (cI) trials. Similarly, reaction times should be slower on iC than on cC trials. We calculated the reaction times for each of the four conditions; the results are shown in Figure 2C.

Consistent with previous data, we found that reactions for iI-trials were significantly faster than for cI trials ($P < 0.001$, $t_{28} > 5.9$; two-tailed t tests) and were also faster for cC-trials than for iC trials ($P < 0.001$, $t_{28} > 5.49$; two-tailed t tests). A two-way ANOVA with "Position1 (congruent/incongruent)" and "Position2 (congruent/incongruent)" as repeated measures revealed a main effect for "Position2" ($F_{1,28} = 18.68$, $P < 0.001$) and a significant "Position1" × "Position2" interaction ($F_{1,28} = 11.95$; $P = 0.002$).

To control for repetition priming effects and their contribution to the Stroop effect, we first calculated reaction times for every condition without repeating trials, i.e., trials with exact the same stimulus. We found a significant increase in reaction times (mean: +13.6 ms, std: 2.6 ms; not shown) for the trials excluding direct repetitions. A three-way ANOVA with "congruency," "semantic-phonetic," and "repetition" (repeated trials vs. excluded) as repeated measures revealed main effects of each factor ("congruency": $F_{1,28} = 9.74$, $P < 0.001$; "semantic-phonetic": $F_{1,28} = 50.93$, $P < 0.001$; "repetition": $F_{1,28} = 55.96$, $P < 0.001$) and a significant "congruency" × "semantic-phonetic" interaction ($F_{1,28} = 115.50$, $P < 0.001$).

We further tested the effect of excluding all repeated trials from the statistics of the behavioral adjustments following conflict and again found that reaction times were increased when compared with the analysis including repeated trials (cC:+29 ms; cI:+1 ms; iI:+2 ms; iC:+59 ms). The increase in reaction times did not change the significance of the different condition interactions. A three-way ANOVA with "repetition," "position1," and "position2" as repeated measures revealed a main effect for "repetition" ($F_{1,28} = 38.98$, $P < 0.001$) and a significant "position1" × "position2" interaction ($F_{1,28} = 59.54$, $P < 0.001$).

FMRI Results

We first investigated regions showing an increased activation during processing of incongruent information in each of the two conditions separately and then compared processing of incongruent items across modalities. In the phonetic condition, the reaction times and accuracy rates indicated that interference occurred during processing of incongruent items (e.g., responding "high" to the word "low" when it was pronounced in high pitch). Indeed, the "incongruent phonetic > congruent phonetic" contrast

A Reaction times

B Percentage of incorrect trials

## C Behavioral adjustments following conflict
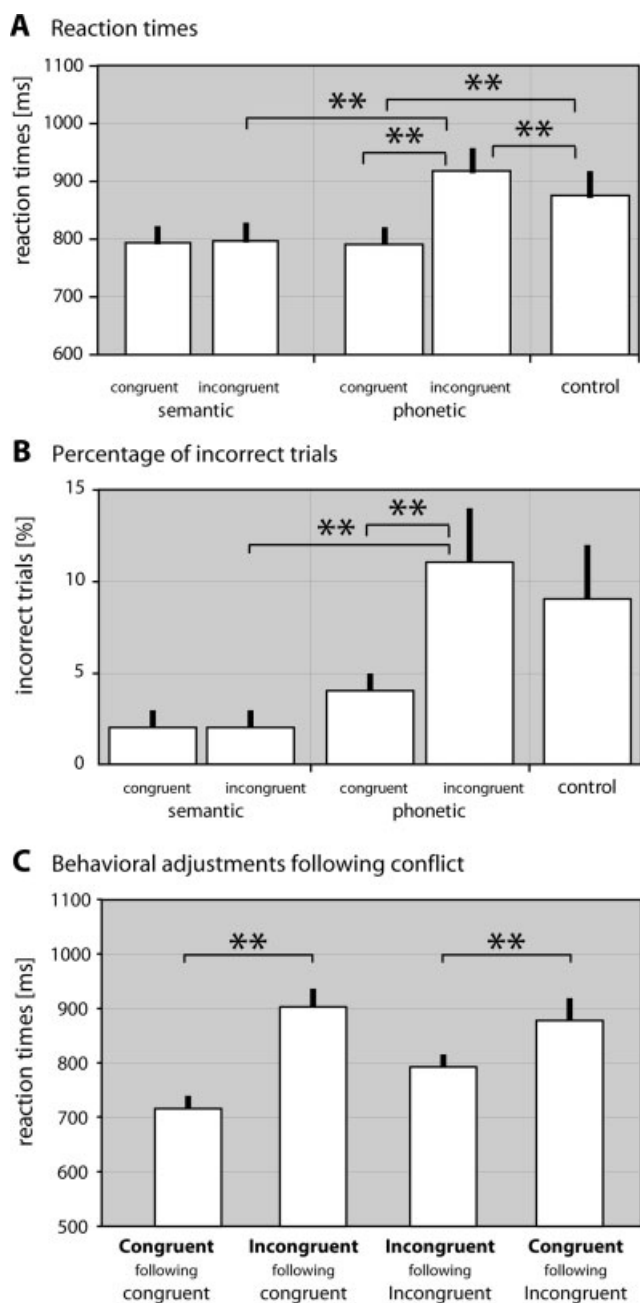
Figure 2.

Behavioral results. (**A**) Reaction times. (**B**) Percentage of incorrect trials. (**C**) Behavioral adjustments following conflict. Previous trial (congruent versus incongruent) by current trial (congruent versus incongruent) interaction.

revealed increased activation in regions previously associated with conflict processing such as the lateral prefrontal cortex (right: MNI coordinates 40/16/32; left: MNI coordinates −48/18/10) and the pre-SMA (MNI coordinates 2/18/46). These regions are shown in Figure 3A. In the

semantic condition, however, the contrast of incongruent vs. congruent items was only associated with increased activation in the precuneus (MNI coordinates: 2/−56/26; Fig. 3B).

Next, the contrast "incongruent phonetic > incongruent semantic" was calculated because exactly identical stimuli (the word "high" spoken in low pitch and the word "low" spoken in high pitch) were used in both conditions. We observed activations in the posterior part of the anterior cingulate cortex (ACC), the medial frontal cortex, left and right dorsolateral prefrontal cortex (DLPFC), thalamus, and the presupplementary motor area (pre-SMA) close to the ACC. The results for the contrast "incongruent phonetic > incongruent semantic" are shown in the Figure 4A, and Table II provides an overview of all significantly activated regions for all contrasts. The parameter estimates shown in Figure 4 demonstrate that the activations are clearly driven by the conflict processing originating from the incongruent phonetic condition.

Regarding the discussion about conflict-adaptation versus priming-effects, we tested how an analysis excluding all repeating trials influences the Stroop-interference activation network. For the second analysis, we removed every event containing a direct repetition of a trial from the regressors of the first analysis. This way we excluded an average of 16% of the trials (from an average of 152 events

A Incongruent phonetic > Congruent phonetic

B Incongruent semantic > Congruent semantic
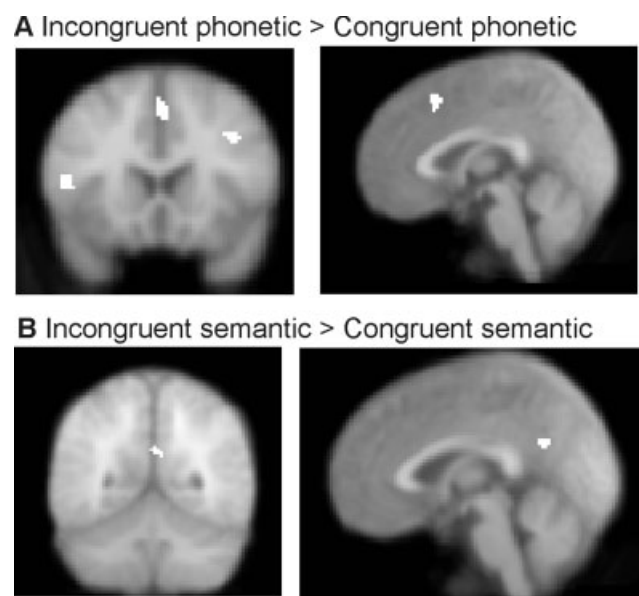
Figure 3.

Conflict processing in the separate domains. (**A**) In the phonetic condition, responding to incongruent items elicited an increased activation in regions previously associated with conflict processing such as the pre-SMA or the lateral prefrontal cortex. (**B**) In the semantic condition, however, the contrast of incongruent vs. congruent items was only associated with increased activation in the precuneus.
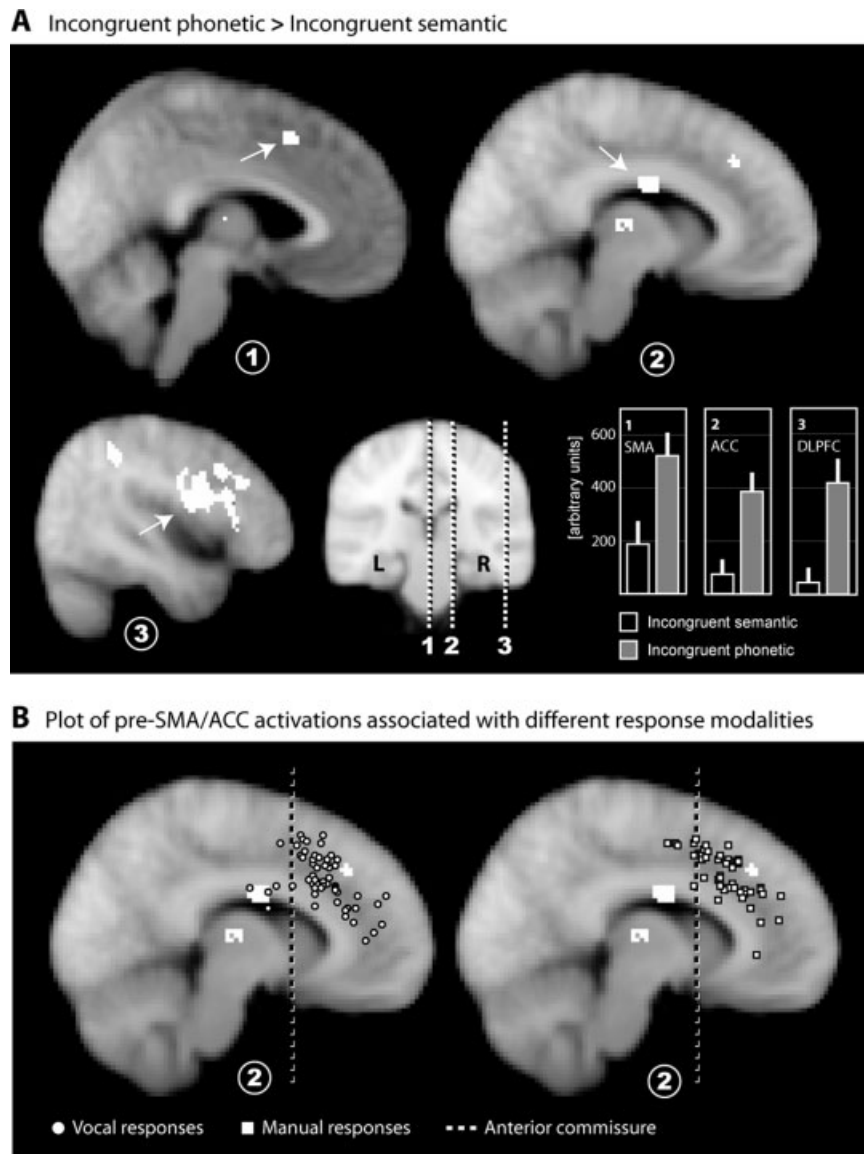
Figure 4.
(**A**) Incongruent phonetic > incongruent semantic. (**B**) Plot reviewing 112 pre-SMA/ACC activations associated with vocal and manual responses. Coordinates were collected and reviewed by Barch and colleagues (Barch et al., 2001) and transferred to MNI space.

to 127). The results revealed activations corresponding to the areas shown in Figure 4A, although the number of activated voxels decreased (ACC 58 to 3; DLPFC 135 to 19; not shown). A comparison of the activation-values for the voxels of the ACC region in the analysis with repetitions and without repetitions across all subjects revealed that the ACC activation without repetitions is significantly smaller ($P = 0.003$, $t_{28} > 3.29$; two-tailed t tests). A critical objection to this result could be the fact that the number of trials for the two analyses did not match. To test this idea, we repeated the first analysis while randomly removing

16% of the trials to match the number of events. Indeed, this revealed a significantly decreased number of activated voxels (ACC 58 to 3; DLPFC 135 to 42; $P < 0.001$, $t_{28} > 3.93$; two-tailed t tests; not shown). Interestingly the activation-values for the analysis without repetitions and the trial-matched analysis did not differ significantly ($P = 0.163$, $t_{28} > 1.43$; two-tailed t tests).

Finally, we aimed at elucidating the mechanism by which the activated clusters participate in a conflict processing network. Interaction of one region with another is reflected in correlated activations in both regions. We thus

TABLE II. Significantly activated regions in the different conditions

| Region | L/R | BA | MNI coordinates | | | z-score |
			x	y	z	
Left DLPFC	**L**	**9**	**−44**	**4**	**20**	**4,9**
White matter	L	—	28	8	28	4,3
Insula	L	13	−34	16	14	3,9
Cingulate gyrus	**L**	**24**	**−6**	**−6**	**26**	**3,9**
Lentiform nucleus	L	—	−18	12	0	3,8
Medial frontal gyrus	L	9	−6	32	38	3,8
Right DLPFC	R	9	48	14	30	3,7
Thalamus	L	—	−6	−16	8	3,7
Anterior cingulate	L	24	−2	32	18	3,7
Cingulate gyrus	L	24	−18	−6	46	3,6
PreSMA	**M**	**6**	**0**	**14**	**48**	**3,6**
Thalamus	L	—	−18	−8	16	3,5
Sub-gyral	L	6	−18	−8	62	3,5
Superior frontal gyrus	M	8	0	30	48	3,4

The table displays the coordinates of the maximally activated voxel in each activation cluster for the "incong. phonetic > incong. semantic" contrast. Bold entries identify connectivity network.

performed functional connectivity analyses using the "psychophysiological interaction" approach [Friston et al., 1997], with a seed region located in the activated posterior part of the ACC (see arrow in Fig. 4A-2). The results show a strong connectivity with the left DLPFC and the pre-SMA (see Fig. 5).

DISCUSSION

Our motivation for implementing the auditory Stroop approach via functional imaging was threefold: (1) Conflict processing might be different in the auditory when compared with the visual domain. We thus wondered whether the neural basis underlying Stroop interference shows modality specific alterations. (2) The ongoing discussion regarding the role of priming in the Stroop task motivated our investigations on the influence of repeating trials on the activity of the conflict processing network. (3) Since the auditory domain is especially affected by certain psychiatric disorders, we discuss the usefulness of an auditory Stroop approach in clinical research.

Conflict Processing in the Auditory as Compared to the Visual Domain

Our major interest in this study was to find out if the use of a different sensory modality in a Stroop interference task would reproduce the common conflict effect in general or if the auditory stimuli per se would result in a different behavioral outcome. Although visual input undergoes a large amount of filtering and reconstruction on the way from the retina to the cortex, auditory information

measures exactly sound frequencies [Hendee and Wells, 1997; Handel, 1989]. This led to our hypothesis that a classical Stroop task used with auditory stimuli should result in a robust conflict effect, whereas at the same time recruiting a network of well-known conflict-related regions, but with adjustments to the different sensory modality.

The results confirm our hypothesis by showing a robust behavioral effect, with a highly significant reaction time difference of about 100 ms between the conflict condition and the other conditions. We found that Stroop interference (as measured by response times and accuracy rates) occurred in the phonetic condition (in which subjects were required to respond against incongruent semantic information), but not in the semantic condition (in which they responded against incongruent pitch information). This result may be most parsimoniously explained by the fact that semantic information is more automatically processed when compared with the naming of pitch information. In other words, conflict in the phonetic condition arises from the fact that the more automatic operation of word processing is suppressed in this condition. This behavioral effect remained significant even after exclusion of all repetition trials (see Fig. 2). The activated network meets our expectations by demonstrating areas well known for conflict management, including the ACC, the DLPFC, the pre-SMA, the medial frontal cortex, and the thalamus.
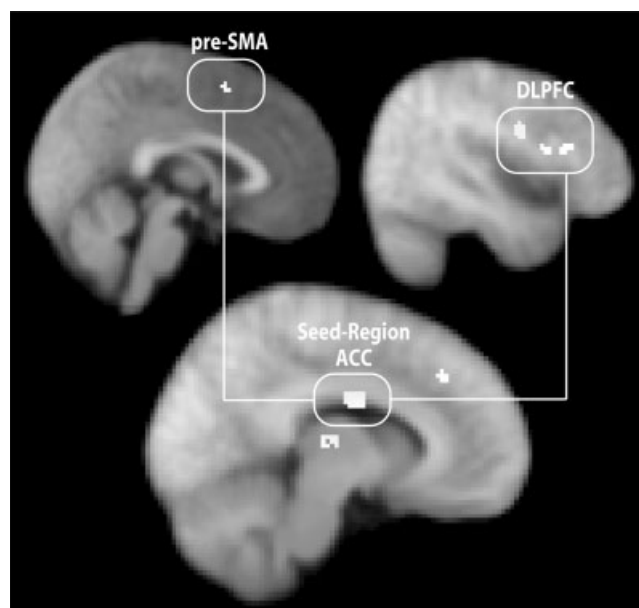
Figure 5.
Connectivity analysis contrast "phonetic > semantic" using the ACC activation (Fig. 4A-2) as seed region. Activity is shown at $P = 0.001$.

Use of different contrasts reveals different levels of conflict processing

The (more conventional) contrast "incongruent phonetic > congruent phonetic" involves incongruent stimuli only in one condition, while task demands are identical in the two conditions. Therefore, this contrast reveals incongruency originating already at the level of stimulus processing. Thus, activation of the pre-SMA/ACC region shown in Figure 3 supports a lower, more stimulus-related level of conflict processing. This region has been observed in a large number of previous studies on the Stroop effect [Barch et al., 2001]. In addition to the contrast "incongruent phonetic > congruent phonetic", the contrast "incongruent phonetic > incongruent semantic" was calculated because exactly identical stimuli (the word "high" spoken in low pitch and the word "low" spoken in high pitch) were used in both conditions. Therefore, the difference in activation revealed by this contrast cannot be explained at the sensory level: The amount of stimulus incongruency is equal in the two conditions, and only task demands differ, so that this contrast reveals conflict at the level of action monitoring and/or response. This contrast activated a particularly posterior and inferior region of the cingulate cortex (Fig. 4A-2) which was previously only observed in a small minority of studies (Fig. 4B).

ACC/pre-SMA

Interestingly, the ACC region activated in the "incongruent phonetic > incongruent semantic" contrast is located at the very posterior/caudal part of the ACC (it should be noted that the maximum difference of the BOLD response is localized to the white matter). This was in contrast to the vast majority of previous studies investigating Stroop interference, conflict, and error detection, which reported activation of more anterior regions of the ACC [Barch et al., 2001]. This even led Barch and colleagues to hypothesize that especially this anterior part of the ACC is more strongly associated with monitoring conflict. However, the ACC activation in our study was revealed in the "incongruent phonetic > incongruent semantic" contrast, while the results from the Stroop tasks discussed in the article by Barch et al. [2001] were based on conventional contrasts of incongruent vs. congruent/neutral trials. While the "incongruent phonetic > incongruent semantic" contrast reflects task-related interference, the conventional "incongruent phonetic > congruent phonetic" contrast may capture both, sensory level and higher-level interference. In the latter contrast, however, the posterior/caudal part of the ACC was not significantly activated at the conventional threshold of $P < 0.001$ (uncorrected).

On the other hand, different response modalities in conflict tasks using oculomotor, manual, and speech responses, activate slightly different ACC regions [Paus et al., 1993; Picard and Strick, 1996], indicating a functional

heterogeneity of the ACC supporting different aspects of cognitive processing. Unfortunately, the general findings related to functional subdivisions of the ACC are heterogeneous. Whereas activation of the caudal region of the ACC is associated with cognitive functions such as attention, for instance detection of an increasing number of stimuli [Posner and Petersen, 1990], the rostral regions of the ACC appear to support the regulation of emotional processing [Bush et al., 2000; Devinsky et al., 1995]. Furthermore, it was proposed that conflict processing and response selection are associated with the activity of the rostral cingulate cortex, while the actual movement execution is linked to the caudal cingulate zone of the ACC [Picard and Strick, 2001]. Interestingly, a recent study using dynamic causal modeling claimed that the intrinsic connectivity between different subregions of the ACC (e.g., the medial cingulate zone and the caudal cingulate zone) is increased during conflict processing to facilitate selection and response execution [Fan et al., 2008].

To visualize the spectrum of conflict-related activations and to further investigate the degree to which the network found in our study differs from previous findings related to conflict processing, we added the locations of another 112 ACC activations to our contrast using coordinates as they were reviewed by Barch et al. [2001]. It is striking that of 112 activations, only 14 (12.5%) are located posterior to the anterior commissure line. Especially, the very posterior and inferior parts of the ACC were exclusively found to be activated in four studies investigating Stroop interference using vocal responses. Based on our data, two interpretations are possible. First, it is possible that increasing integration of the auditory sense in conflict processing results in a posterior/caudal and inferior/ventral shift of ACC activity due to the different sensory modality. Alternatively, the specific activation differing from the majority of previous studies may be due to task-related interference in the "incongruent phonetic > incongruent semantic" contrast. Findings from a recent study, [Roberts and Hall, 2008] directly comparing visual and auditory Stroop tasks rather support the second interpretation. In this study, very similar activations within the pre-SMA/ACC region were observed in both modalities based on the conventional Stroop contrast and no additional activations in other (posterior and caudal) ACC regions were reported.

The activation of the pre-SMA during the incongruent condition may appear surprising at first sight, because the SMA and pre-SMA regions are more commonly reported from studies involving complex motor control tasks [for review see Picard and Strick, 1996]. Nevertheless, activation of the pre-SMA has been reported in numerous studies involving cognitive control [Barch et al., 2001; Ikeda et al., 1999; Zysset et al., 2001], and also appears frequently in Stroop interference tasks, without being always clearly characterized. One reason for that may lie in the fact that the terminology in this historically old research field is often not compelling. The pre-SMA is sometimes reported as rostral/anterior dorsal ACC [e.g., Bush et al., 2002;

Critchley et al., 2005] or in combination with the rostral/anterior dorsal ACC [Braver et al., 2001; Holroyd et al., 2004; Milham et al., 2002; Ruff et al., 2001]. The fact that we found significant correlation between activity in the posterior inferior cingulate cortex and the pre-SMA region (see Fig. 5 and discussion below), further suggests that these regions support similar processes.

DLPFC

Together with the ACC, the DLPFC is the most commonly reported region in Stroop interference tasks. It has been suggested that if a conflict is detected by the ACC, a cognitive control system located in the DLPFC is alerted, which is responsible for reducing conflict by biasing information processing toward successful task completion [Botvinick et al., 2001]. Accordingly, neuroimaging studies have shown the engagement of the left and right DLPFC in executive functioning, and more specifically during selective attention [Durston et al., 2003; Kerns et al., 2004; MacDonald et al., 2000; Milham et al., 2003] and attention-related and conflict-related activity [Weismann et al., 2004]. While the DLPFC is a critical component of the decision-making network recruited for the Stroop interference task, its activation seems to be independent of response modality [Heekeren et al., 2006]. A modality specific adjustment of activity of the DLPFC is not described for conflict interference, but greater activation of the same DLPFC area was observed during an auditory compared with the visual working memory task [Crottaz-Herbette et al., 2004]. Results from a divided attention task (involving competing auditory and visual stimuli) have revealed, that the activity of the DLPFC is more strongly modulated by the performance of the subjects (poor performers recruit more DLPFC in an attempt to improve performance), than by the actual sensory modality [Johnson and Zatorre, 2006].

Additional regions

In addition to the ACC, the DLPFC and the pre-SMA region where an increased activation in the "Incongruent phonetic" when compared with the "incongruent semantic" condition can be relatively easy explained by the enhanced interference in this condition [because of response competition; Treisman and Fearnley, 1969]. However, as indicated in Table II, we also found significant effects in other regions. Most of these activations could be attributed to enhanced conflict processing in the incongruent phonetic condition. The enhanced activity in the "white matter" (MNI coordinates −28; 8; 28) may be attributable to the adjacent left middle frontal gyrus, which is part of the DLPFC (see above). Activation of the insula was also previously observed in the Stroop task, but is probably related to a more general mechanism and not specifically to interference, because it was also observed during processing of infrequent items [Leung et al., 2000].

The lentiform nucleus comprises the putamen and the globus pallidus within the basal ganglia. Both structures are relevant for motor and executive functions; in situations where conflicting information is being processed, motor outputs related to one type of response patterns need to be selected, which is related to inhibition of the putamen by frontal and parietal regions [e.g., Jaffard et al., 2008]. Thus, the increased activation of the lentiform nucleus in the "incongruent phonetic > incongruent semantic" condition might be due to this enhancement of inhibitory GABAergic action within the putamen [for a discussion of the complex relationship between inhibitory neural signaling and the BOLD signal, see Logothetis, 2008]. Enhanced neural metabolism in the Stroop task was also found in the thalamus using PET imaging [Ravnkilde et al., 2002] and is most likely related to the increased attentional demands during processing of incongruent information [Carter et al., 1995]. Furthermore, results from several studies suggest that activity in the thalamus is actually necessary for coping with interfering information, because patients with thalamic infarcts [Shim et al., 2008] and after thalamotomy [Schuurman et al., 2002] are indeed impaired in the Stroop task. Finally, the increased activity in the superior frontal gyrus (and in the "sub-gyral" region at MNI coordinates of −18/−8/62, which is also close to the superior frontal gyrus) might also be part of the prefrontal control network.

Functional connectivity

The power in the "incongruent phonetic > incongruent semantic" contrast was not high enough to show a significant functional connectivity, however, we were able to show the connectivity-network for the more general "phonetic > semantic" contrast. The connectivity analysis demonstrated that a network including the ACC, the pre-SMA, and the DLPFC is recruited for control and adjustment of the behavior during conflict processing. Several recent studies using functional connectivity are in accordance with the results of our connectivity analysis.

Functional connectivity of the ACC with the pre-SMA and the DLPFC was shown for the "interference-related" condition of a Stroop color-word paradigm [Harrison et al., 2005], for a counting Stroop paradigm [Zheng and Rajapakse, 2006], respectively, supported by recent findings in a study of ACC resting-state functional connectivity [Marguilies et al., 2007].

The strong correlation between the activity of the caudal ACC and the lateral prefrontal cortex as well as medial frontal gyrus, particularly the region of the pre-SMA, is also consistent with a meta-analysis of functional connectivity of the ACC within the human frontal lobe [Koski and Paus, 2000]. These findings are further supported by the results of several studies in monkeys. Using neuronal tracers, it has been demonstrated that both the primary [Morecraft and Van Hoesen, 1992] and supplementary [Bates and Goldman-Rakic, 1993] motor areas are densely interconnected with the caudal ACC.

Sensory-Level vs. Task-Related Interference

In addition to the contrast "incongruent phonetic > incongruent semantic," we also analyzed the conventional incongruent > congruent contrasts separately for the semantic and the phonetic condition (see Fig. 3). As expected, we found an increased activation in regions associated with conflict processing only in the phonetic condition, where reaction times and accuracy rates indicated interference, but not in the semantic condition. However, no activation of the anterior cingulate cortex was observed in these contrasts. This divergence with the results from the "incongruent phonetic > incongruent semantic" contrast shown in Figure 4 may be explained by the different levels of interference: The "classical" Stroop contrast (incongruent vs. congruent trials separately for the semantic and the phonetic condition) compares trials with differential interference already at the level of sensory processing (e.g., the word "High" pronounced in low pitch when compared with the word "High" pronounced in high pitch). Therefore, interference occurs already at the sensory level and not only at higher processing levels. On the other hand, the contrast "incongruent phonetic > incongruent semantic" compares trials with an equal amount of sensory interference which differ with regard to response interference, because incongruent phonetic trials require subjects to respond against the more automatic response (based on semantic processing), whereas in incongruent semantic trials, subjects can respond in line with their automatic response. The finding that the anterior cingulate cortex was activated only in the "incongruent phonetic > incongruent semantic" contrast but not in the "incongruent phonetic > congruent phonetic" contrast might therefore be explained by an important role of this region for the resolution of response-based interference, but not for sensory interference [Barch et al., 2001; Zysset et al., 2001].

Influence of Stimulus Repetition

We found that an exclusion of repeating trials results in significantly increased reaction times for all conditions but did not eliminate the Stroop effect. The results for the behavioral adjustment following conflict are only slightly influenced by the exclusion of repeating trials and do not change their significance. This result could be explained by both the conflict theory and stimulus-specific repetition priming. The recruitment of frontal cognitive control would as well result in faster reactions as the utilization of priming related memories. Using the data from fMRI, we found that an analysis without trial repetitions resulted in significantly lower activations of the conflict areas than an analysis with all trials. An additional analysis with the same number of trials as the actual stimulus repetitions randomly removed confirmed that this effect was rather due to the reduced trial number, than a trial repetition effect. Both trial-reduced analyses were significantly differ-

ent from the original analysis, but their activation values did not differ significantly from each other. These results suggest that processing of the repeating trials is most likely not related to priming effects, because events related to priming activity should not reduce power in an area assigned to conflict monitoring in the same way as randomized chosen events do. While these findings support the conflict adjustment theory more than they do the priming theory, the interpretation of a null finding (no difference between the data after removal of repeated inconsistent trials when compared with the data after random removal of an equal number of trials) should, of course, always be regarded cautiously. We cannot exclude the possibility that the lack of a difference might not be due to a lack of power. Further studies are necessary to confirm these results.

The Auditory Stroop Approach for Clinical Purposes

It has been shown that the ability to perform tasks related to conflict management is altered in bipolar patients [Kronhaus et al., 2006], patients with, e.g., attention-deficit/hyperactivity disorder [Lansbergen et al., 2007] or in paranoid schizophrenia [Henik and Salo, 2004; Nordahl et al., 2001; Strauss, 1993]. Among the different sensory modalities, the auditory modality is of particular interest for schizophrenia [Veuillet et al., 2001], because schizophrenia particularly affects auditory processing [Bentaleb et al., 2002]. While processing deficits of the visual domain are typically evoked by structural brain damages [Prigatano and Wong, 1999], auditory verbal hallucinations are one of the most characteristic symptoms of schizophrenia [David, 1999]. Furthermore, recent studies have shown that patients with schizophrenia, who frequently experience auditory hallucinations, exhibit dysfunctions of the ACC and bilateral temporal lobe [Cleghorn et al., 1992; Shergill et al., 2000], respectively, do not show activation of the ACC during Stroop task performance [Carter et al., 1997]. Many studies also reported abnormalities in the generation of preattentive automatic processing of auditory stimuli (e.g., mismatch negativity) in schizophrenia [for overview see Umbricht and Krljes, 2005]. Furthermore, a recent study has shown that patients with schizophrenia performed worse on an auditory emotional perception task than participants from other groups [Vaskinn et al., 2007]. Since our Stroop task showed a very robust behavioral effect for the auditory modality, the suggested version of the Stroop interference task may be particularly useful for clinical investigations.

Stroop results in the trial-by-trial version may be used for the discrimination of different subtypes of schizophrenia. Although the undifferentiated subtype exhibited an increased facilitation effect for congruent stimuli, the paranoid subtype showed an increased interference effect for incongruent stimuli [Carter et al., 1993]. Here, we have described an auditory Stroop experiment showing very

robust behavioral effects in healthy subjects. Both the deficits in auditory and in attentional/conflict processing of schizophrenia patients are relevant for the auditory version of the Stroop task. Therefore, auditory Stroop results may represent even more sensitive trait markers for schizophrenia or may be even better suited to differentiate schizophrenia subtypes than conventional findings. Hence, the suggested version of the Stroop interference task may be particularly useful for clinical investigations.

CONCLUSIONS

This study aimed at investigating the neural correlates of a newly developed auditory approach to the Stroop interference task using fMRI. The auditory Stroop design created a robust Stroop interference effect, producing significantly longer reaction times for the conflict related condition. Excluding repeating trials did not change the behavioral as well as fMRI results, when compared with a matched number of randomly chosen trials. Although the vast majority of visual Stroop interference tasks resulted in the activations of the anterior/dorsal part of the ACC, we describe a posterior/ventral activation of the ACC in the contrast of incongruent phonetic vs. incongruent semantic trials, which is strictly due to task-related interference. In contrast, the conventional comparison of incongruent phonetic vs. congruent phonetic trials activated a region in the pre-SMA/ACC, which was also reported in several visual Stroop studies. Finally, a connectivity analysis revealed that the three most significantly activated areas in the "incongruent phonetic vs. incongruent semantic" contrast (ACC, DLPFC, and pre-SMA) constitute a conflict processing network with highly correlated activity.

ACKNOWLEDGMENTS

REFERENCES

Banich MT, Milham MP, Jacobson BL, Webb A, Wszalek T, Cohen NJ, Kramer AF (2001): Attentional selection and the processing of task-irrelevant information: Insights from fMRI examinations of the Stroop task. Prog Brain Res 134:459–470.

Barch DM, Braver TS, Akbudak E, Conturo T, Ollinger J, Snyder A (2001): Anterior cingulate cortex and response conflict: Effects of response modality and processing domain. Cereb Cortex 11:837–848.

Bates JF, Goldman-Rakic PS (1993): Prefrontal connections of medial motor areas in the rhesus monkey. J Comp Neurol 336:211–228.

Becker TM, Kerns JG, Macdonald AW, Carter CS (2008): Prefrontal dysfunction in first-degree relatives of schizophrenia patients during a Stroop task. Neuropsychopharmacology 33:2619–2625.

Bentaleb LA, Beauregard M, Liddle P, Stip E (2002): Cerebral activity associated with auditory verbal hallucinations: A functional magnetic resonance imaging case study. J Psychiatry Neurosci 27:110–115.

Botvinick M, Nystrom LE, Fissell K, Carter CS, Cohen JD (1999): Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature 402:179–181.

Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD (2001): Conflict monitoring and cognitive control. Psychol Rev 108: 624–652.

Braver TS, Barch DM, Gray JR, Molfese DL, Snyder A (2001): Anterior cingulate cortex and response conflict: Effects of frequency, inhibition and errors. Cereb Cortex 11:825–836.

Bush G, Luu P, Posner MI (2000): Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 4:215–222.

Bush G, Vogt BA, Holmes J, Dale AM, Greve D, Jenike MA, Rosen BR (2002): Dorsal anterior cingulate cortex: A role in reward-based decision making. Proc Natl Acad Sci USA 99:523–528.

Carter CS, Mintun M, Cohen JD (1995): Interference and facilitation effects during selective attention: An H215O PET study of Stroop task performance. Neuroimage 2:264–272.

Carter CS, Robertson LC, Nordahl TE, O'Shora-Celaya LJ, Chaderjian MC (1993): Abnormal processing of irrelevant information in schizophrenia: The role of illness subtype. Psychiatry Res 48:17–26.

Carter CS, Mintun M, Nichols T, Cohen JD (1997): Anterior cingulate gyrus dysfunction and selective attention deficits in schizophrenia: [15O]H2O PET study during single-trial Stroop task performance. Am J Psychiatry 154:1670–1675.

Carter CS, Macdonald AM, Botvinick M, Ross LL, Stenger VA, Noll D, Cohen JD (2000): Parsing executive processes: Strategic vs. evaluative functions of the anterior cingulate cortex. Proc Natl Acad Sci USA 97:1944–1948.

Cleghorn JM, Franco S, Szechtman B, Kaplan RD, Szechtman H, Brown GM, Nahmias C, Garnett ES (1992): Toward a brain map of auditory hallucinations. Am J Psychiatry 149:1062–1069.

Critchley HD, Tang J, Glaser D, Butterworth B, Dolan RJ (2005): Anterior cingulate activity during error and autonomic response. Neuroimage 27:885–895.

Crottaz-Herbette S, Anagnoson RT, Menon V (2004): Modality effects in verbal working memory: Differential prefrontal and parietal responses to auditory and visual stimuli. Neuroimage 21:340–351.

David AS (1999): Auditory hallucinations: Phenomenology, neuropsychology and neuroimaging update. Acta Psychiatr Scand Suppl 395:95–104.

Devinsky O, Morrell MJ, Vogt BA (1995): Contributions of anterior cingulate cortex to behaviour. Brain 118 (Part 1):279–306.

Durston S, Davidson MC, Thomas KM, Worden MS, Tottenham N, Martinez A, Watts R, Ulug AM, Casey BJ (2003): Parametric manipulation of conflict and response competition using rapid mixed-trial event-related fMRI. Neuroimage 20:2135–2141.

Dyer FN, Severance LJ (1973): Stroop interference with successive presentations of separate incongruent words and colors. J Exp Psychol 98:438–439.

Erickson KI, Milham MP, Colcombe SJ, Kramer AF, Banich MT, Webb A, Cohen NJ (2004): Behavioral conflict, anterior cingulate cortex, and experiment duration: Implications of diverging data. Hum Brain Mapp 21:98–107.

Fan J, Hof PR, Guise KG, Fossella JA, Posner MI (2008): The functional integration of the anterior cingulate cortex during conflict processing. Cereb Cortex 18:796–805.

Filbey FM, Toulopoulou T, Morris RG, McDonald C, Bramon E, Walshe M (2008): Selective attention deficits reflect increased genetic vulnerability to schizophrenia. Schizophr Res 101:169–175.

Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ (1997): Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 6:218–219.

Gehring WJ, Knight RT (2000): Prefrontal-cingulate interactions in action monitoring. Nat Neurosci 3:516–520.

Handel S (1989): Listening. New York: MIT Press.

Harrison BJ, Shaw M, Yucel M, Purcell R, Brewer WJ, Strother SC, Egan GF, Olver JS, Nathan PJ, Pantelis C (2005): Functional connectivity during Stroop task performance. Neuroimage 24:181–191.

Heekeren HR, Marrett S, Ruff DA, Bandettini PA, Ungerleider LG (2006): Involvement of human left dorsolateral prefrontal cortex in perceptual decision making is independent of response modality. Proc Natl Acad Sci USA 103:10023–10028.

Hendee WR, Wells PN (1997): The Perception of Visual Information. New York: Springer-Verlag.

Henik A, Salo R (2004): Schizophrenia and the Stroop effect. Behav Cogn Neurosci Rev 3:42–59.

Holroyd CB, Nieuwenhuis S, Yeung N, Nystrom L, Mars RB, Coles MGH, Cohen JD (2004): Dorsal anterior cingulate cortex shows fMRI response to internal and external error signals. Nat Neurosci 7:497–498.

Huynh H, Feldt L (1976): Estimation of the box correction for degrees of freedom from sample data in the randomized block and split-plot designs. J Educ Stat 1:69–82.

Ikeda A, Yazawa S, Kunieda T, Ohara S, Terada K, Mikuni N, Nagamine T, Taki W, Kimura J, Shibasaki H (1999): Cognitive motor control in human pre-supplementary motor area studied by subdural recording of discrimination/selection-related potentials. Brain 122 (Part 5):915–931.

Jaffard M, Longcamp M, Velay JL, Anton JL, Roth M, Nazarian B, Boulinguez P (2008): Proactive inhibitory control of movement assessed by event-related fMRI. Neuroimage 42:1196–1206.

Jenkinson M, Bannister P, Brady M, Smith S (2002): Improved optimization for the robust and accurate linear registration and motion correction of brain images. Neuroimage 17:825–841.

Johnson JA, Zatorre RJ (2006): Neural substrates for dividing and focusing attention between simultaneous auditory and visual events. Neuroimage 31:1673–1681.

Kerns JG, Cohen JD, MacDonald AW III, Cho RY, Stenger VA, Carter CS (2004): Anterior cingulate conflict monitoring and adjustments in control. Science 303:1023–1026.

Koski L, Paus T (2000): Functional connectivity of the anterior cingulate cortex within the human frontal lobe: A brain-mapping meta-analysis. Exp Brain Res 133:55–65.

Kronhaus DM, Lawrence NS, Williams AM, Frangou S, Brammer MJ, Williams SCR, Andrew CM, Phillips ML (2006): Stroop performance in bipolar disorder: Further evidence for abnormalities in the ventral prefrontal cortex. Bipolar Disord 8:28–39.

Lansbergen MM, Kenemans JL, van Engeland H (2007): Stroop interference and attention-deficit/hyperactivity disorder: A review and meta-analysis. Neuropsychology 21:251–262.

Leboe LC, Mondor TA (2007): Item-specific congruency effects in nonverbal auditory Stroop. Psychol Res 71:568–575.

Leung HC, Skudlarski P, Gatenby JC, Peterson BS, Gore JC (2000): An event-related functional MRI study of the stroop color word interference task. Cereb Cortex 10:552–560.

Logothetis NK (2008): What we can do and what we cannot do with fMRI. Nature 453:869–878.

MacDonald AW III, Cohen JD, Stenger VA, Carter CS (2000): Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288:1835–1838.

MacLeod CM (1991): Half a century of research on the Stroop effect: An integrative review. Psychol Bull 109:163–203.

Margulies DS, Kelly AMC, Uddin LQ, Biswal BB, Castellanos FX, Milham MP (2007): Mapping the functional connectivity of anterior cingulate cortex. Neuroimage 37:579–588.

Mayr U, Awh E, Laurey P (2003): Conflict adaptation effects in the absence of executive control. Nat Neurosci 6:450–452.

McClain L (1983): Stimulus-response compatibility affects auditory Stroop interference. Percept Psychophys 33:266–270.

Milham MP, Banich MT, Webb A, Barad V, Cohen NJ, Wszalek T, Kramer AF (2001): The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. Brain Res Cogn Brain Res 12:467–473.

Milham MP, Erickson KI, Banich MT, Kramer AF, Webb A, Wszalek T, Cohen NJ (2002): Attentional control in the aging brain: Insights from an fMRI study of the Stroop task. Brain Cogn 49:277–296.

Milham MP, Banich MT, Barad V (2003): Competition for priority in processing increases prefrontal cortex's involvement in top-down control: An event-related fMRI study of the stroop task. Brain Res Cogn Brain Res 17:212–222.

Miller EK, Cohen JD (2001): An integrative theory of prefrontal cortex function. Annu Rev Neurosci 24:167–202.

Morecraft RJ, Van Hoesen GW (1992): Cingulate input to the primary and supplementary motor cortices in the rhesus monkey: Evidence for somatotopy in areas 24c and 23c. J Comp Neurol 322:471–489.

Nieuwenhuis S, Stins JF, Posthuma D, Polderman TJC, Boomsma DI, de Geus EJ (2006): Accounting for sequential trial effects in the flanker task: Conflict adaptation or associative priming? Mem Cognit 34:1260–1272.

Nordahl TE, Carter CS, Salo RE, Kraft L, Baldo J, Salamat S, Robertson L, Kusubov N (2001): Anterior cingulate metabolism correlates with stroop errors in paranoid schizophrenia patients. Neuropsychopharmacology 25:139–148.

Pardo JV, Pardo PJ, Janer KW, Raichle ME (1990): The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. Proc Natl Acad Sci USA 87:256–259.

Paus T, Petrides M, Evans AC, Meyer E (1993): Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: A positron emission tomography study. J Neurophysiol 70:453–469.

Paus T (2001): Primate anterior cingulate cortex: Where motor control, drive and cognition interface. Nat Rev Neurosci 2:417–424.

Peterson BS, Skudlarski P, Gatenby JC, Zhang H, Anderson AW, Gore JC (1999): An fMRI study of Stroop word-color interference: Evidence for cingulate subregions subserving multiple distributed attentional systems. Biol Psychiatry 45:1237–1258.

Picard N, Strick PL (1996): Motor areas of the medial wall: A review of their location and functional activation. Cereb Cortex 6:342–353.

Picard N, Strick PL (2001): Imaging the premotor areas. Curr Opin Neurobiol 11:663–672.

Posner MI, Petersen SE (1990): The attention system of the human brain. Annu Rev Neurosci 13:25–42.

Prigatano GP, Wong JL (1999): Cognitive and affective improvement in brain dysfunctional patients who achieve inpatient rehabilitation goals. Arch Phys Med Rehabil 80:77–84.

Ravnkilde B, Videbech P, Rosenberg R, Gjedde A, Gade A (2002): Putative tests of frontal lobe function: A PET-study of brain activation during Stroop's test and verbal fluency. J Clin Exp Neuropsychol 24:534–547.

Roberts KL, Hall DA (2008): Examining a supramodal network for conflict processing: A systematic review and novel functional

magnetic resonance imaging data for related visual and auditory stroop tasks. J Cogn Neurosci 20:1063–1078.

Ruff CC, Woodward TS, Laurens KR, Liddle PF (2001): The role of the anterior cingulate cortex in conflict processing: Evidence from reverse Stroop interference. Neuroimage 14:1150–1158.

Schuurman PR, Bruins J, Merkus MP, Bosch DA, Speelman JD (2002): A comparison of neuropsychological effects of thalamotomy and thalamic stimulation. Neurology 59:1232–1239.

Shergill SS, Brammer MJ, Williams SC, Murray RM, McGuire PK (2000): Mapping auditory hallucinations in schizophrenia using functional magnetic resonance imaging. Arch Gen Psychiatry 57:1033–1038.

Shim YS, Kim JS, Shon YM, Chung YA, Ahn KJ, Yang DW (2008): A serial study of regional cerebral blood flow deficits in patients with left anterior thalamic infarction: Anatomical and neuropsychological correlates. J Neurol Sci 266:84–91.

Shor RE (1975): An auditory analog of the Stroop test. J Gen Psychol 93:281–288.

Smith SM (2002): Fast robust automated brain extraction. Hum Brain Mapp 17:143–155.

Strauss M (1993): Relations of symptoms to cognitive deficits in schizophrenia. Schizophr Bull 19:215–231.

Stroop JR (1935): Studies of interference in serial verbal reaction. J Exp Psychol 18:643–662.

Treisman A, Fearnley S (1969): The Stroop test: Selective attention to colours and words. Nature 222:437–439.

Umbricht D, Krljes S (2005): Mismatch negativity in schizophrenia: A meta-analysis. Schizophr Res 76:1–23.

Vaskinn A, Sundet K, Friis S, Simonsen C, Birkenaes AB, Engh JA, Jonsdottir H, Ringen PA, Opjordsmoen S, Andreassen OA (2007): The effect of gender on emotion perception in schizophrenia and bipolar disorder. Acta Psychiatr Scand 116:263–270.

Veuillet E, Georgieff N, Philibert B, Dalery J, Marie-Cardine M, Collet L (2001): Abnormal peripheral auditory asymmetry in schizophrenia. J Neurol Neurosurg Psychiatry 70:88–94.

Weissman DH, Warner LM, Woldorff MG (2004): The neural mechanisms for minimizing cross-modal distraction. J Neurosci 24:10941–10949.

Woolrich MW, Ripley BD, Brady M, Smith SM (2001): Temporal autocorrelation in univariate linear modeling of FMRI data. Neuroimage 14:1370–1386.

Zheng X, Rajapakse JC (2006): Learning functional structure from fMR images. Neuroimage 31:1601–1613.

Zysset S, Muller K, Lohmann G, von Cramon DY (2001): Color-word matching stroop task: Separating interference and response conflict. Neuroimage 13:29–36.